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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,510	LE ET AL.	
	Examiner	Art Unit	
	JACOB CHEU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-44 and 47-68* is/are pending in the application.

4a) Of the above claim(s) *13-43 and 50-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,44,47-49 and 64-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/8/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's filed amendments on 5/26/2009 has been received and entered into record.

2. Claims 13-43 and 50-63 are withdrawn further consideration.

3. Claims 1-3, 6-12, 44, 47-49 and 64-68 are under examination. Claims 1-3, 6-44, 47-68 are pending.

4. The previous rejection on claims 1-12, 44-49 under 35 USC 112, first paragraph are withdrawn because Applicant has amended claim satisfying enablement requirement.

5. However, a new ground of rejection is set forth in this Office Action (see below).

Election/Restrictions

Applicant elected species malondialdehyde-modified low density lipoprotein (MDA-LDL) for examination. Applicant argues that there is no serious burden on Examiner to search the rest of the species. Examiner would like to point out that each of the species has patentably distinct physical, chemical and biological characteristics. It would involve different class/subclass, and diverse fields of non-patent literature. Thus, the election is deemed proper and Final.

Claim Rejections - 35 USC § 112

Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 68 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The present invention provides methods utilizing the fat-induced antibody response (FIAR) to assess endothelial function. Additional methods are provided that utilize FIAR for diagnosing and monitoring the progression of vascular diseases, and as a measure of the oxidative stress imposed upon vascular endothelium. The state of art involves immunoassay and pathological evaluation.

Monitoring progression of the vascular disease

In view of the disclosure, Applicant collected coronary artery patients' samples and conducted various treatments and measurements. Applicant performed the recited method, i.e. administering polyunsaturated fatty acid, monounsaturated fatty acid, saturated fatty acid and no-fat diet to the selected patients (See Example 4; Section 0085-Section 0088). Figure 6 shows the auto-antibody recognizes modified (oxidatively modified) low density lipoprotein. It appears the level of antibody increases in the selected 10 patients. Figure 7 is a statistical normalized graph of the time versus level of triglycerides. Figure 7 presents a profile for different diet treatment. It is noted that the polyunsaturated fatty acid (panel C) has an increase trend within FIVE hours and decreases at the SIXTH hour. FIG. 8 shows normalized auto-antibody levels following all four different diets. Panel A depicts the transient decrease in antibody levels following the polyunsaturated fat meal.

Based upon the above experiments and data, it is not sufficient to enable one artisan in the field to use the *recited* steps for *diagnosing* and *monitoring* the progression of an vascular disease (emphasis added).

First, there is no study on the so-called "correlation" with the "progression" on the vascular disease (emphasis added). The parameters Applicant measured are triglycerides and modified LDL antibody. The correlation Applicant indeed conducted is the normalization of the triglycerides and the antibody levels (See Figure 7-8). There is lack of study on severity. For instance, Applicant discusses the atherosclerotic lesion category based on its progression in Table 1. Nevertheless, no correlation was made with such atherosclerotic lesion score. In addition, the overall time course for the instant study is merely based on a SIX-hour short term study. Applicant even terms this as "transient" change/response (See Section 0086). It is known to the ordinary skill in the field that severity is a specific term and usually is not applicable for such a short period of time. It is noted that Figure 8 shows some decrease of the level of antibody from zero hour (about 1.00 value) to 2 hour and an increase back to approximately 0.95 value from 2-4 hour and level off a little bit to approximately 0.90 from 4-6 hour. It is not known whether the levels of the antibody would back up again or not. Particularly, the preamble of the current claims direct to monitoring the *progression* of the vascular disease, more further researches, i.e. at least longer period of time, are needed to further verify/characterize the progression and diagnosing of the vascular disease.

Scope of Enablement

3. Claims 1, 4-12, 64-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cardiovascular disease, does not reasonably provide enablement for other all vascular diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As discussed above, it is noted that Applicant uses ELISA assay to determine the level of low density lipoprotein in the biological samples from the patients (See Example 5; Section 0089-0095). The data and normalized results are shown in Figures 6-8 are from patients suffering atherosclerosis. It is known that vascular disease is a genus. This genus also includes lymphedema, blood clotting disorder, venous blood clots, varicose veins. Thus fart, Applicant merely presented one species clinical evidence, namely atherosclerosis. Given the fact that the unpredictability of diagnosing a complex disease, undue experiments would have to be implemented in order to substantiate the aforementioned other species to justify the whole genus.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, 6-8,12, 44, 47-49 and 64-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Le et al. (Metabolism 2000 Vol. 49, page 1271-1277; Applicant submitted IDS).

> Le et al. teach a method of diagnosing cardiovascular disease, i.e. atherosclerosis, in patients. Le et al. teach measuring the difference of the MAD-LDL (malondialdehyde-modified low-density lipoprotein) autoantibodies at different time period in the cardiovascular patients who have been fed with polyunsaturated food, e.g. Lipomul (from cottonseed; also Le et al. discuss the contribution of polyunsaturated fatty acid to the results), also containing triglyceride (See Abstract; page 1272, right column, second paragraph; Figures 4-5). The measurement of the autoantibodies are conducted by ELISA by the IgG-LDL complex. Supra.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Le et al. in view of Billman et al. (Circulation 1999 Vol. 99, page 2452-2457).

Le et al. reference has been discussed, and Le et al. teach administering fat-loaded food orally. Le et al. also attribute the reduction of autoantiobyd of the oxidative lipoprotein to the polyunsaturated fatty acid. However, Le et al. do not teach using intravenously phospholip emulsion administering.

Billman et al. teach using intravenously phospholip emulsion administering polyunsaturated fatty acid to subjects for study cardiovascular disease (See Abstract and Materials/Methods). Intravenously phospholip emulsion administering polyunsaturated fatty acid is well-known, widely practiced since it provides advantage of bypassing GI delivery/digestion/absorption route (see page 2455, left column, first column). Such merely requires routine skill in the art.

Therefore, it would have been prima facie obvious to one ordinary skill in the art at the time the invention was made to have motivated Le et al. to use alternative intravenous administering method, such as taught by Billman et al., to study the reduction of the autoantibody agains MDA-LDL associated with polyunsaturated fatty acid. By using this technique one artisan can eliminate complexity of GI delivery/digestion/absorption and simply focus on the circulatory results from blood samples.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACOB CHEU whose telephone number is (571)272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacob Cheu/
Examiner, Art Unit 1641